



Smith-Lemli-Opitz syndrome

Smith-Lemli-Opitz syndrome is a developmental disorder that affects many parts of the body. This condition is characterized by distinctive facial features, small head size (microcephaly), intellectual disability or learning problems, and behavioral problems. Many affected children have the characteristic features of autism, a developmental condition that affects communication and social interaction. Malformations of the heart, lungs, kidneys, gastrointestinal tract, and genitalia are also common. Infants with Smith-Lemli-Opitz syndrome have weak muscle tone (hypotonia), experience feeding difficulties, and tend to grow more slowly than other infants. Most affected individuals have fused second and third toes (syndactyly), and some have extra fingers or toes (polydactyly).

The signs and symptoms of Smith-Lemli-Opitz syndrome vary widely. Mildly affected individuals may have only minor physical abnormalities with learning and behavioral problems. Severe cases can be life-threatening and involve profound intellectual disability and major physical abnormalities.

Frequency

Smith-Lemli-Opitz syndrome affects an estimated 1 in 20,000 to 60,000 newborns. This condition is most common in whites of European ancestry, particularly people from Central European countries such as Slovakia and the Czech Republic. It is very rare among African and Asian populations.

Genetic Changes

Mutations in the *DHCR7* gene cause Smith-Lemli-Opitz syndrome.

The *DHCR7* gene provides instructions for making an enzyme called 7-dehydrocholesterol reductase. This enzyme is responsible for the final step in the production of cholesterol. Cholesterol is a waxy, fat-like substance that is produced in the body and obtained from foods that come from animals (particularly egg yolks, meat, poultry, fish, and dairy products). Cholesterol is necessary for normal embryonic development and has important functions both before and after birth. It is a structural component of cell membranes and the protective substance covering nerve cells (myelin). Additionally, cholesterol plays a role in the production of certain hormones and digestive acids.

Mutations in the *DHCR7* gene reduce or eliminate the activity of 7-dehydrocholesterol reductase, preventing cells from producing enough cholesterol. A lack of this enzyme also allows potentially toxic byproducts of cholesterol production to build up in the blood, nervous system, and other tissues. The combination of low cholesterol levels

and an accumulation of other substances likely disrupts the growth and development of many body systems. It is not known, however, how this disturbance in cholesterol production leads to the specific features of Smith-Lemli-Opitz syndrome.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- 7-Dehydrocholesterol reductase deficiency
- RSH Syndrome
- SLO syndrome
- SLOS

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Smith-Lemli-Opitz syndrome
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0175694/>

Other Diagnosis and Management Resources

- GeneReview: Smith-Lemli-Opitz Syndrome
<https://www.ncbi.nlm.nih.gov/books/NBK1143>

General Information from MedlinePlus

- Diagnostic Tests
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy
<https://medlineplus.gov/drugtherapy.html>
- Genetic Counseling
<https://medlineplus.gov/geneticcounseling.html>
- Palliative Care
<https://medlineplus.gov/palliativecare.html>
- Surgery and Rehabilitation
<https://medlineplus.gov/surgeryandrehabilitation.html>

Additional Information & Resources

MedlinePlus

- Health Topic: Developmental Disabilities
<https://medlineplus.gov/developmentaldisabilities.html>
- Health Topic: Lipid Metabolism Disorders
<https://medlineplus.gov/lipidmetabolismdisorders.html>

Genetic and Rare Diseases Information Center

- Smith-Lemli-Opitz syndrome
<https://rarediseases.info.nih.gov/diseases/5683/smith-lemli-opitz-syndrome>

Educational Resources

- Disease InfoSearch: Smith-Lemli-Opitz Syndrome
<http://www.diseaseinfosearch.org/Smith-Lemli-Opitz+Syndrome/6648>
- Genetic Science Learning Center, University of Utah
<http://learn.genetics.utah.edu/content/disorders/singlegene/>
- Kennedy Krieger Institute
<https://www.kennedykrieger.org/patient-care/diagnoses-disorders/smith-lemli-opitz-syndrome>
- MalaCards: smith-lemli-opitz syndrome
http://www.malacards.org/card/smith_lemli_opitz_syndrome
- My46 Trait Profile
<https://www.my46.org/trait-document?trait=Smith-Lemli-Opitz%20syndrome&type=profile>
- Orphanet: Smith-Lemli-Opitz syndrome
http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=818
- Swedish Information Center for Rare Diseases
<http://www.socialstyrelsen.se/rarediseases/smith-lemli-opitzsyndrome>

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD)
<https://rarediseases.org/rare-diseases/smith-lemli-opitz-syndrome/>
- Resource list from the University of Kansas Medical Center
<http://www.kumc.edu/gec/support/smith-le.html>
- Smith-Lemli-Opitz/RSH Foundation
<http://www.smithlemliopitz.org/>

GeneReviews

- Smith-Lemli-Opitz Syndrome
<https://www.ncbi.nlm.nih.gov/books/NBK1143>

ClinicalTrials.gov

- ClinicalTrials.gov
<https://clinicaltrials.gov/ct2/results?cond=%22smith-lemli-opitz+syndrome%22>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28Smith-Lemli-Opitz+Syndrome%5BMAJR%5D%29+AND+%28Smith-Lemli-Opitz+syndrome%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D>

OMIM

- SMITH-LEMLI-OPITZ SYNDROME
<http://omim.org/entry/270400>

Sources for This Summary

- GeneReview: Smith-Lemli-Opitz Syndrome
<https://www.ncbi.nlm.nih.gov/books/NBK1143>
- Jira PE, Waterham HR, Wanders RJ, Smeitink JA, Sengers RC, Wevers RA. Smith-Lemli-Opitz syndrome and the DHCR7 gene. *Ann Hum Genet.* 2003 May;67(Pt 3):269-80. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/12914579>
- Nowaczyk MJ, Waye JS, Douketis JD. DHCR7 mutation carrier rates and prevalence of the RSH/Smith-Lemli-Opitz syndrome: where are the patients? *Am J Med Genet A.* 2006 Oct 1;140(19):2057-62. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/16906538>
- Nowaczyk MJ, Waye JS. The Smith-Lemli-Opitz syndrome: a novel metabolic way of understanding developmental biology, embryogenesis, and dysmorphology. *Clin Genet.* 2001 Jun;59(6):375-86. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/11453964>
- Porter FD. RSH/Smith-Lemli-Opitz syndrome: a multiple congenital anomaly/mental retardation syndrome due to an inborn error of cholesterol biosynthesis. *Mol Genet Metab.* 2000 Sep-Oct;71(1-2):163-74. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/11001807>

- Sikora DM, Pettit-Kekel K, Penfield J, Merkens LS, Steiner RD. The near universal presence of autism spectrum disorders in children with Smith-Lemli-Opitz syndrome. *Am J Med Genet A*. 2006 Jul 15;140(14):1511-8.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/16761297>
 - Yu H, Patel SB. Recent insights into the Smith-Lemli-Opitz syndrome. *Clin Genet*. 2005 Nov;68(5):383-91. Review. Erratum in: *Clin Genet*. 2005 Dec;68(6):570.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/16207203>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1350989/>
-

Reprinted from Genetics Home Reference:

<https://ghr.nlm.nih.gov/condition/smith-lemli-opitz-syndrome>

Reviewed: July 2007

Published: March 21, 2017

Lister Hill National Center for Biomedical Communications

U.S. National Library of Medicine

National Institutes of Health

Department of Health & Human Services